UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
OFFICE OF PREVENTION, PESTICIDES, AND TOXIC SUBSTANCES
WASHINGTON, D.C. 20460

MEMORANDUM

DATE: August 12, 2003

SUBJECT: **Lactofen.** Revisions to HED Tolerance Reassessment Risk Assessment.
DP Barcode: D292794 PC Code: 128888

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Introduction:

This memo updates the HED Chapter for the Reregistration Eligibility Decision Document for lactofen (D269621, October 12, 2000). The only changes to the risk assessment are new cancer risk estimates based on the new cancer classifications of lactofen and its metabolite acifluorofen. As described below, there are no cancer concerns from lactofen or acifluorfen exposure by any route or pathway.

The cancer classification for lactofen was changed after the Mechanism of Toxicity Assessment Review Committee (MTARC) reviewed new data and concluded that peroxisome proliferation was supported as the mode of action of lactofen-induced liver tumors in rodents. The MTARC (TXR 014590, March 12, 2001 report) evaluated the data according to criteria from the International Life Sciences Institute. The Cancer Assessment Review Committee reclassified lactofen in light of these new data (TXR 0050184, May 21, 2002 report), and the conclusions of the MTARC.

Discussion:

The **previous** cancer classification of lactofen was "Group B2, probable human carcinogen", cancer risk was assessed using a Q_1*.

The **present** cancer classification is "likely to be carcinogenic to humans at high enough doses to cause these biochemical and histopathological effects in livers of rodents but unlikely to be carcinogenic at doses below those causing these changes". Human cancer risk is now assessed by a margin of exposure (MOE) approach, using a NOAEL = 0.3 mg/kgbw/day and margin of exposure of 100. A cancer risk assessment is required only for chronic or long term exposures.

The revised dietary cancer risk estimate for the U.S. general population for lactofen is summarized below. The exposure level used was that previously employed for the chronic dietary risk assessment for lactofen.

$$\text{Cancer MOE} = \frac{\text{NOAEL}}{\text{Exposure}} = \frac{0.3 \text{ mg/kgbw/day}}{1\text{x}10^{-6} \text{ mg/kgbw/day}} = 300{,}000$$

Since the estimated dietary cancer risk is well above the target MOE = 100, there are no concerns for cancer risk from chronic exposure to lactofen in food.

The following table summarizes drinking water cancer risks for lactofen.

Cancer NOAEL (mg/kgbw/day)	Target MOE	Target exposure (mg/kgbw/day)	Food + residential exposure (mg/kgbw/day)	Max drinking water exposure (mg/kgbw/day)	EEC - PRZM/ EXAMS (ug/L)	EEC - SCI-GROW (ug/L)	DWLOC (ug/L)
0.3	100	0.003	$1\text{x}10^{-6}$	0.003	0.022	0.006	105

Since the Estimated Environmental Concentrations (EECs) are well below the Drinking Water Level of Comparison (DWLOC), cancer risks from lactofen in drinking water are not of concern.

There are no concerns from chronic residential or occupational exposure because chronic exposure by these pathways is not expected.

Dietary drinking water risks from acifluorofen resulting from lactofen applications were discussed in the review of Kit Farwell, D.V.M. (7/14/03). The assessment considered the recent cancer reclassification of acifluorofen as a peroxisome proliferator with risk quantification using an MOE approach. The following was concluded:

> *Cancer risks from drinking water exposure were evaluated both from exposure to the herbicide, sodium acifluorfen, and from exposure to acifluorfen as a degradate of the herbicide, lactofen. There were no concerns for cancer risk by exposure from either source because the drinking water level of comparison (DWLOC) for chronic exposure was greater than estimated drinking water concentrations (EDWCs) for acifluorfen from either source.*

Please refer to that review for further information regarding acifluorofen resulting from lactofen applications.

Acifluorofen is not considered a significant metabolite of lactofen in foods, so acifluorofen risks from this source are not expected.

Conclusions:

There are no cancer concerns from lactofen or acifluorfen exposure by any route or pathway. This risk assessment update can be used to support the Tolerance Reassessment decision as well as the new uses and tolerances for cotton and peanuts. Although the assessment is based on use of a 3X FQPA safety factor for a missing rabbit developmental study (applied only to the acute dietary assessment for females 13-50), aggregate risks would still be acceptable even if a 10X factor were applied, since the dietary food risk is <0.1% of the aPAD, and the acute DWLOC is over 1000-fold greater than the highest EEC.

BIBLIOGRAPHY

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